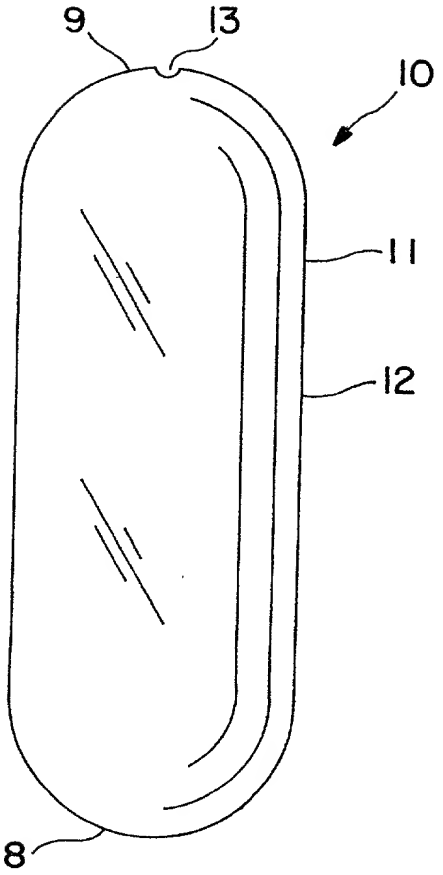

FIG. 1

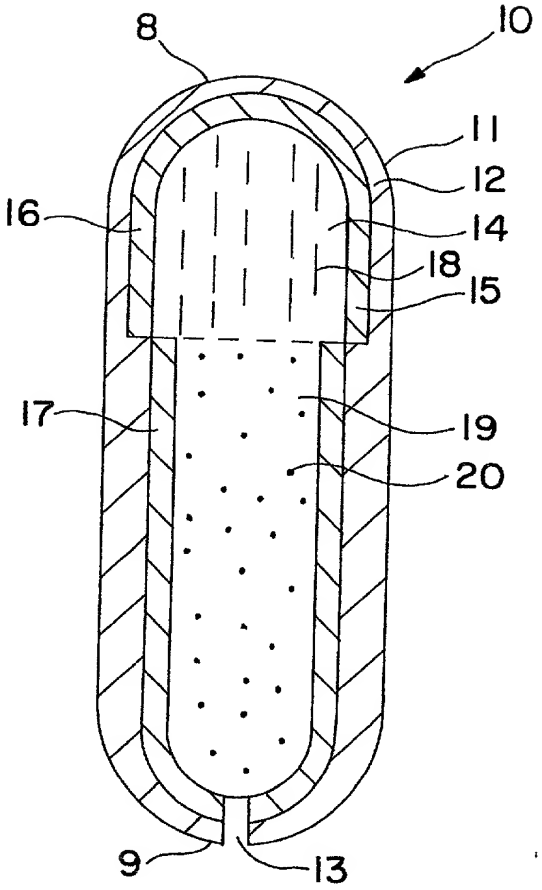

FIG. 2

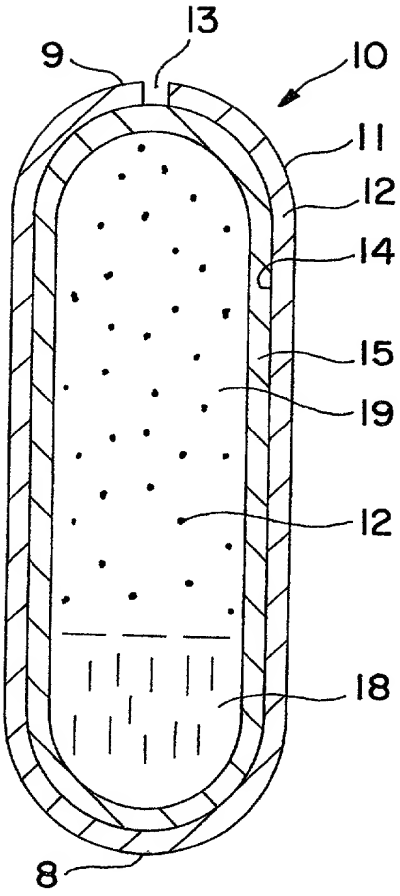

FIG. 3

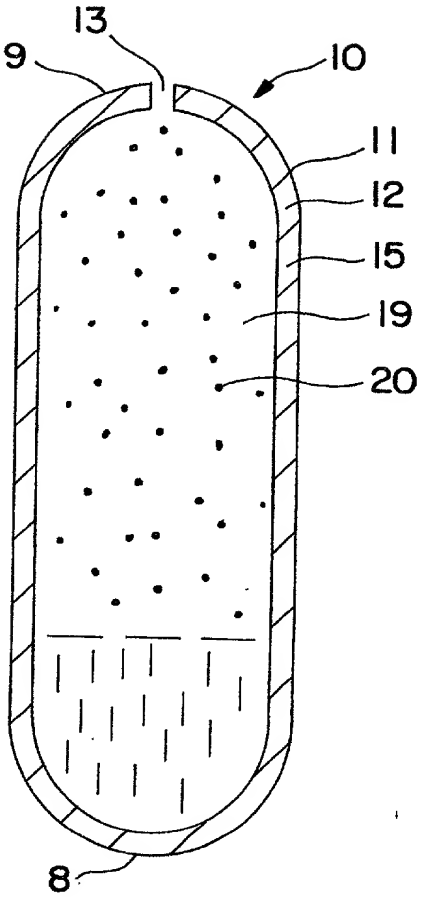

FIG. 4

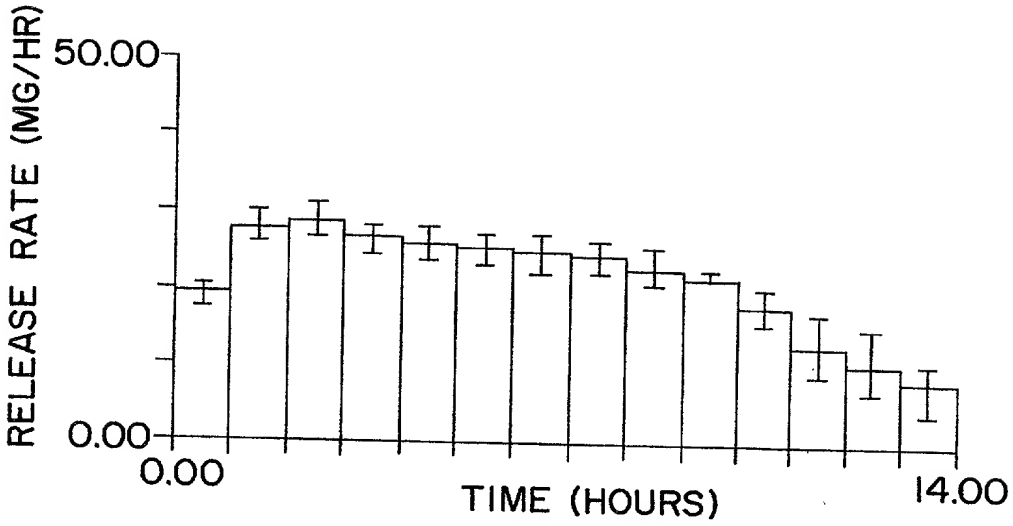
RELEASE RATE (MG/HR)
50.00
0.00
0.00
TIME (HOURS)
14.00

FIG. 5A

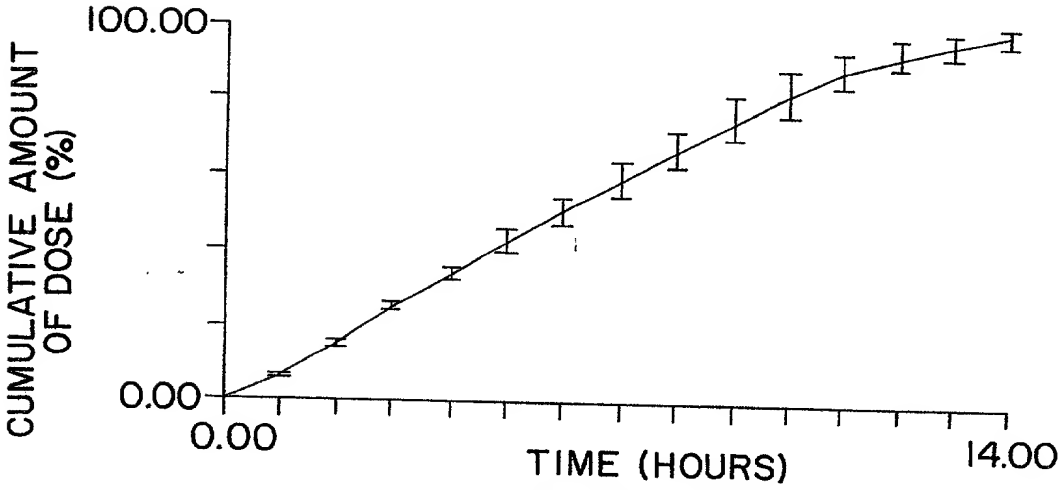
CUMULATIVE AMOUNT OF DOSE (%)
100.00
0.00
0.00
TIME (HOURS)
14.00

FIG. 5B

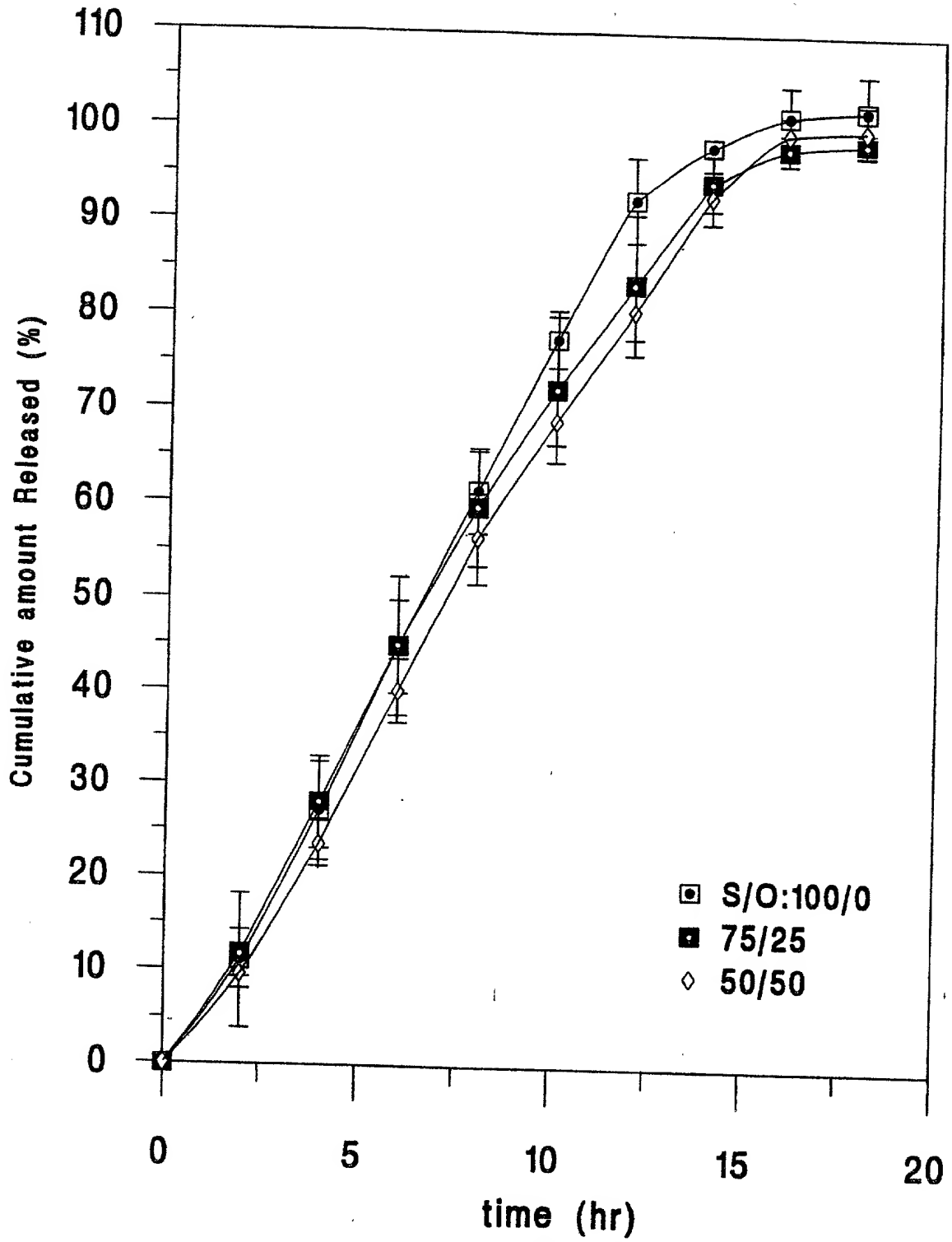
110
100
90
80
70
60
50
40
30
20
10
0
Cumulative amount Released (%)
0
5
10
15
20
time (hr)
S/O:100/0
75/25
50/50

FIG. 6

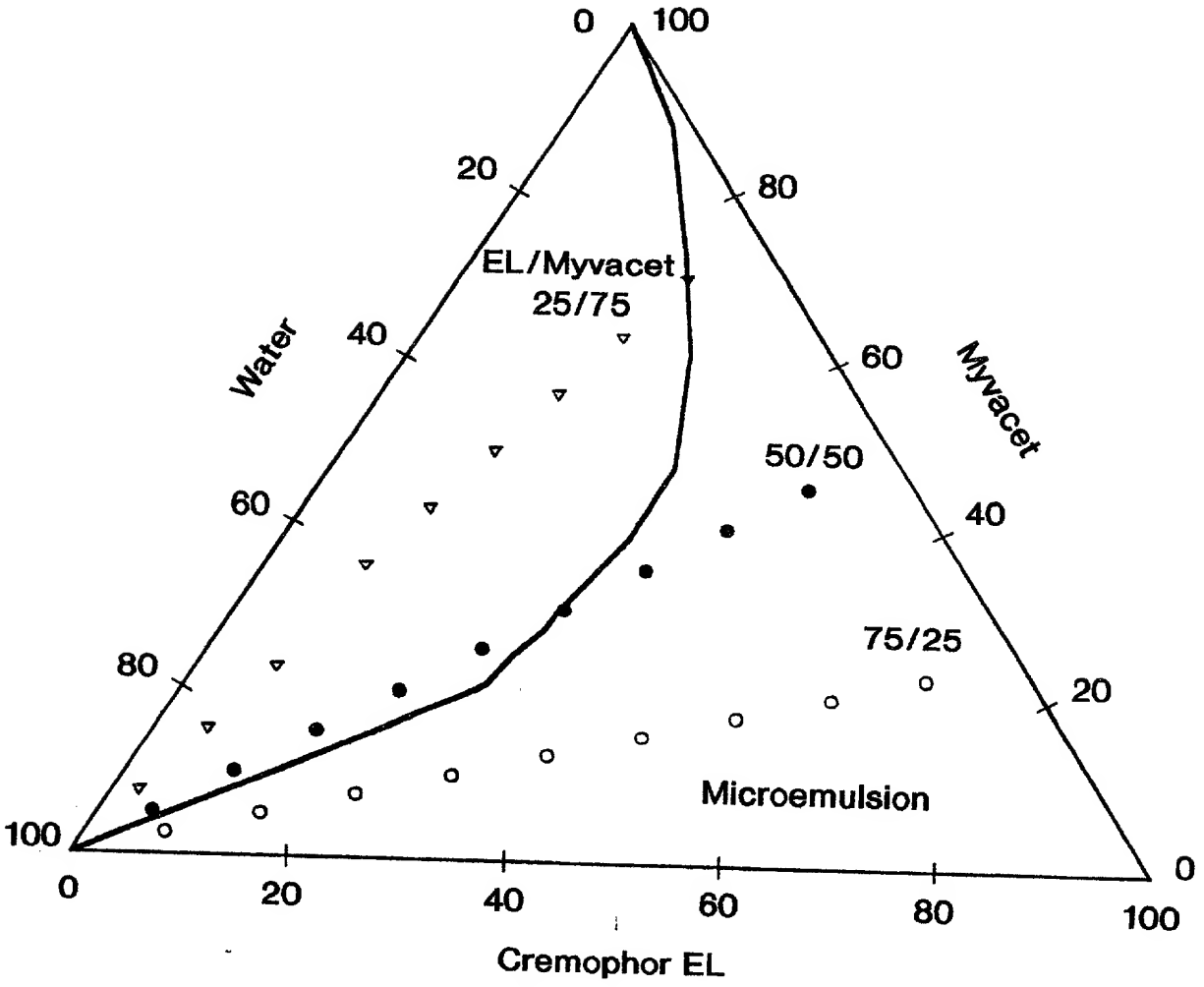
0
100
20
80
EL/Myvacet
25/75
Water
40
60
Myvacet
50/50
60
40
75/25
80
20
Microemulsion
100
0
0
20
40
60
80
100
Cremophor EL

FIG. 7

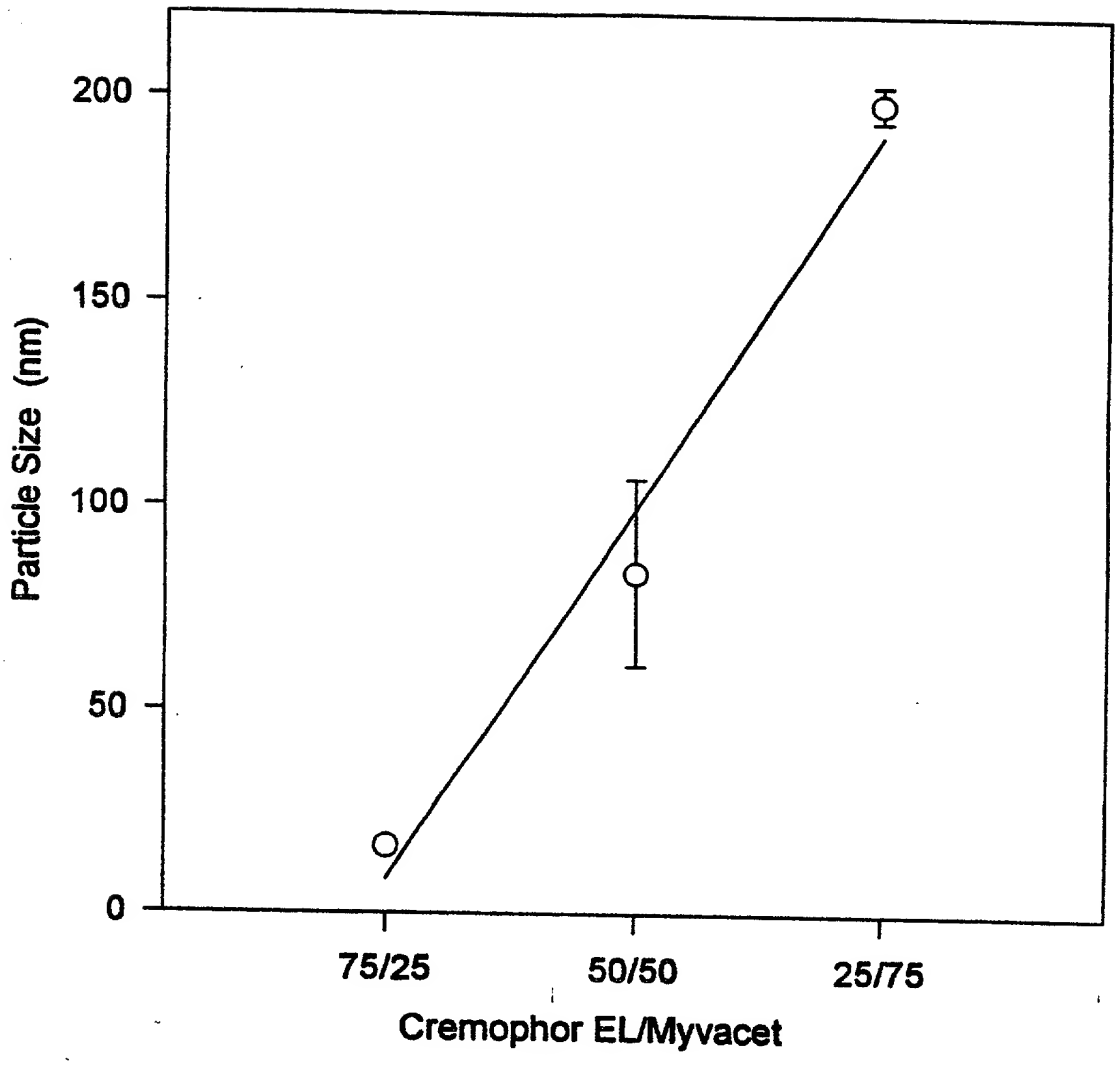
200
150
100
50
0
Particle Size (nm)
75/25
50/50
25/75
Cremophor EL/Myvacet

FIG. 8

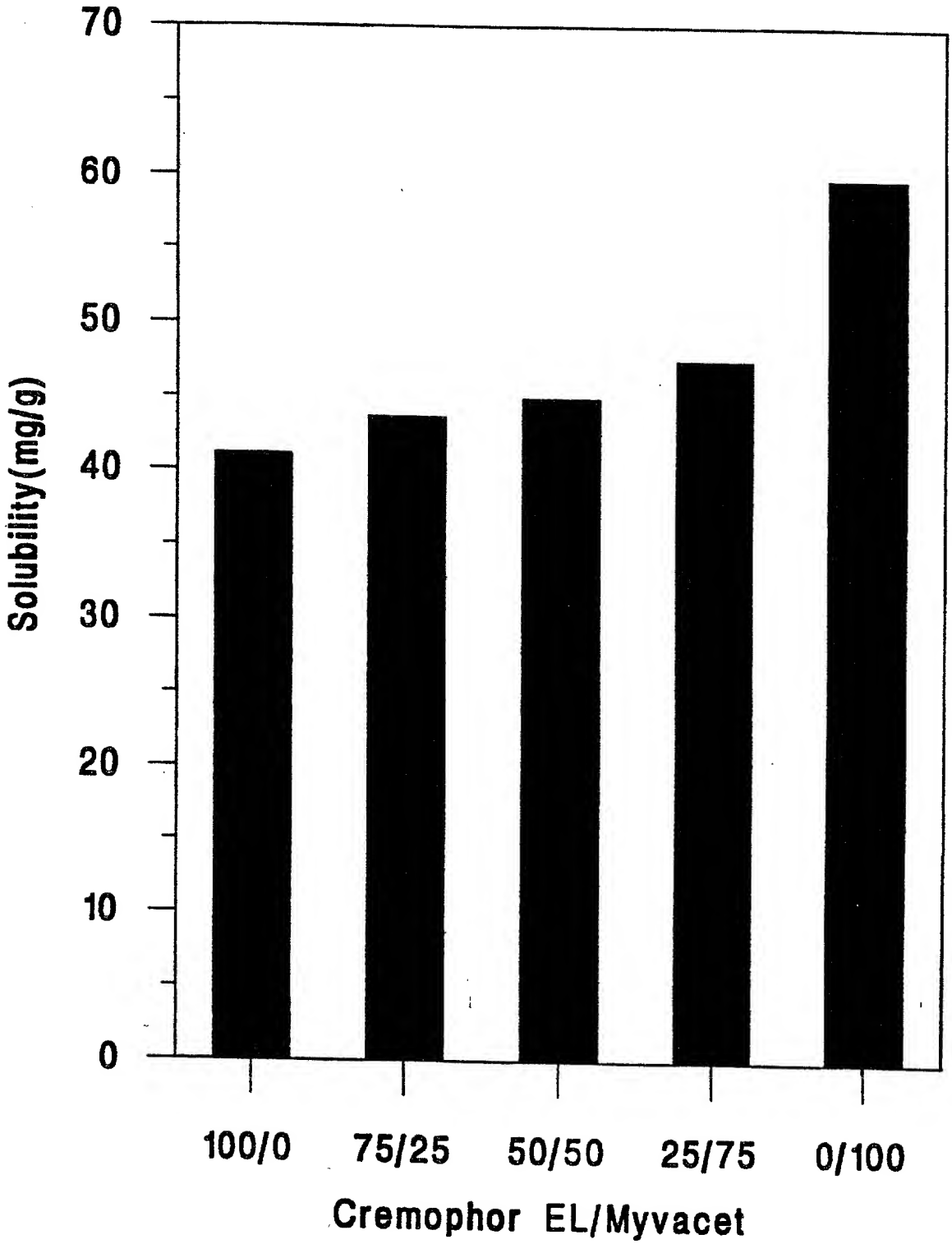
70
60
50
40
30
20
10
0
Solubility(mg/g)
100/0
75/25
50/50
25/75
0/100
Cremophor EL/Myvacet

FIG. 9

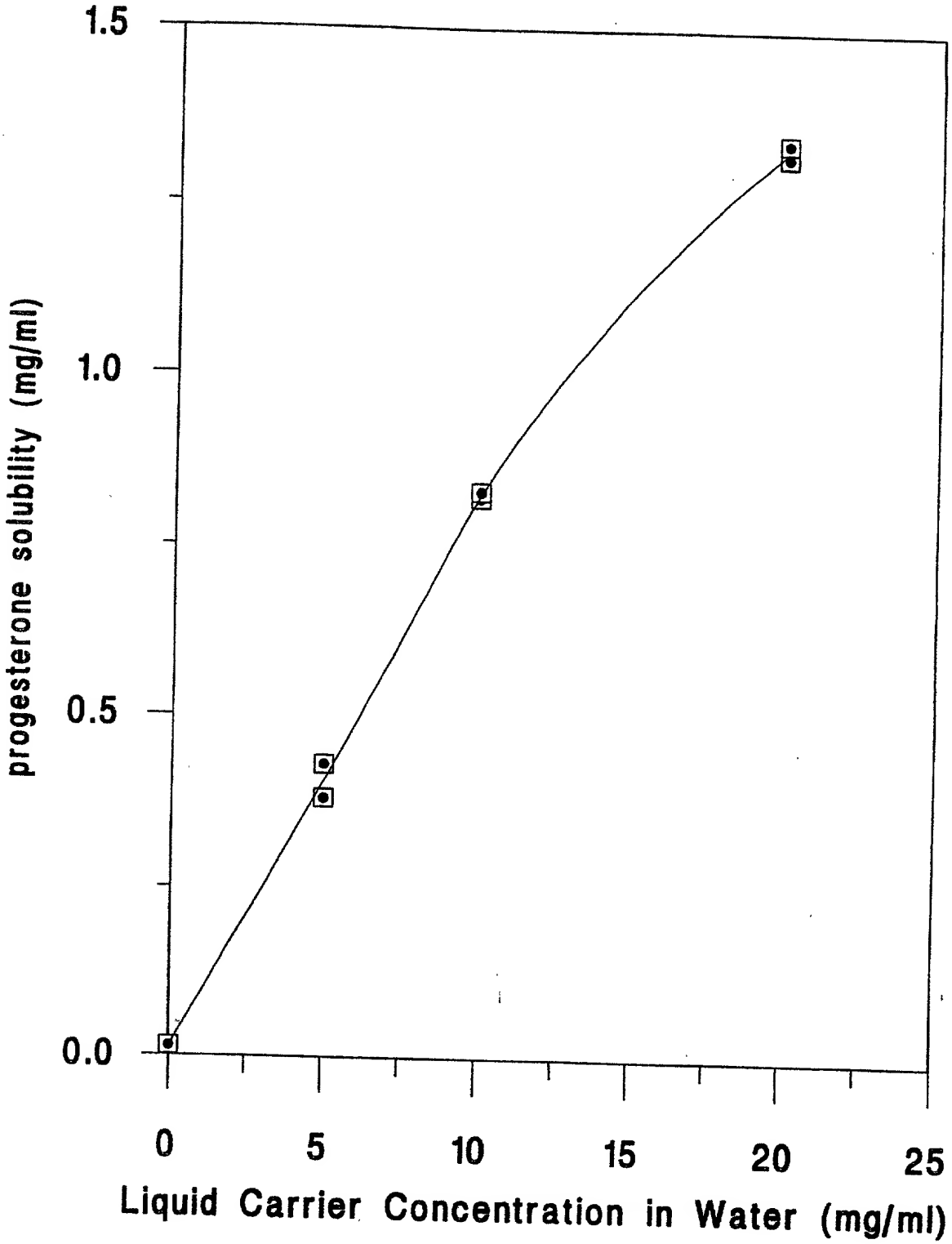
1.5
1.0
0.5
0.0
progesterone solubility (mg/ml)
0
5
10
15
20
25
Liquid Carrier Concentration in Water (mg/ml)

FIG. 10

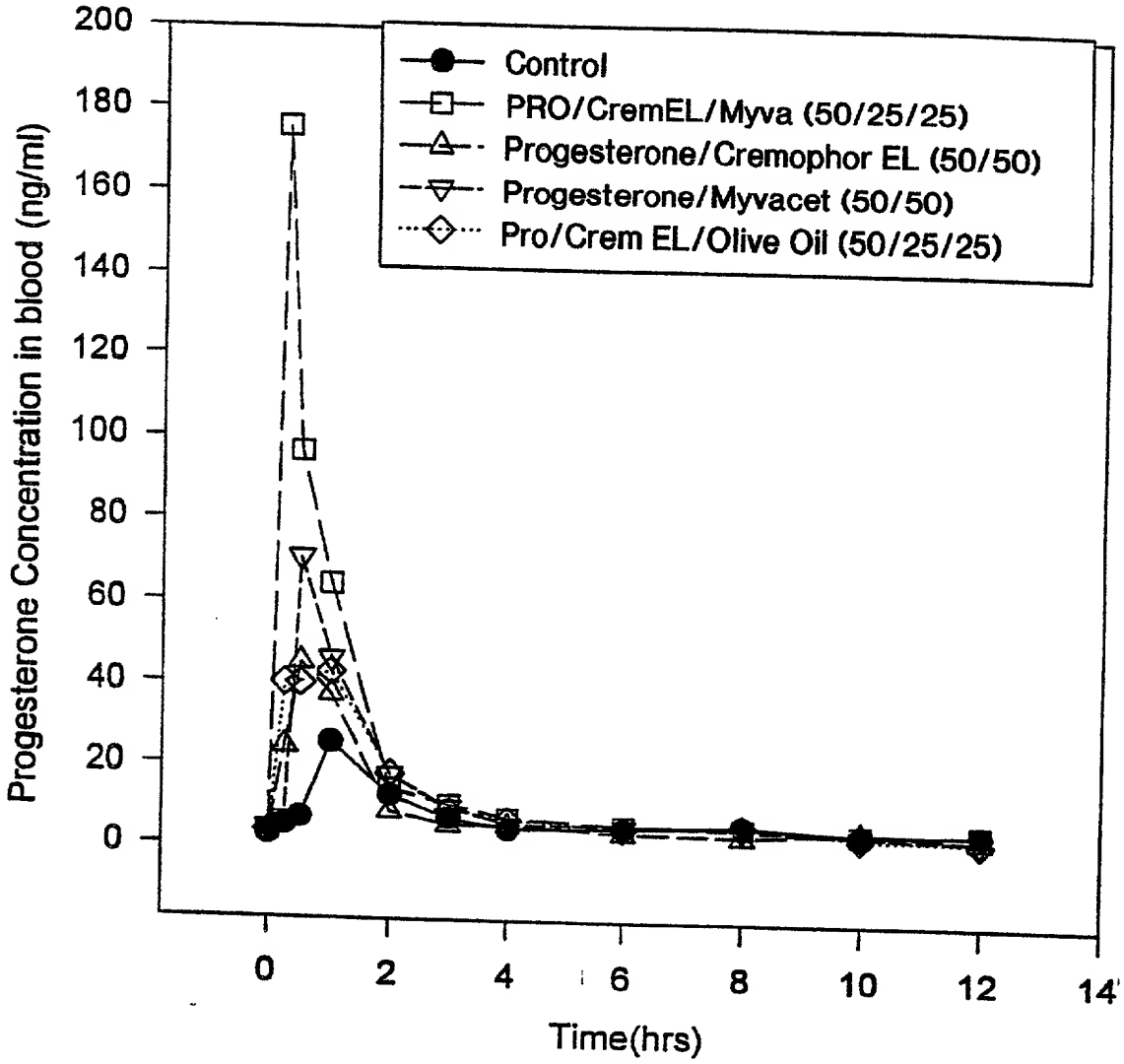
Control
PRO/CremEL/Myva (50/25/25)
Progesterone/Cremophor EL (50/50)
Progesterone/Myvacet (50/50)
Pro/Crem EL/Olive Oil (50/25/25)
Progesterone Concentration in blood (ng/ml)
200
180
160
140
120
100
80
60
40
20
0
0
2
4
6
8
10
12
14
Time(hrs)

FIG. 11

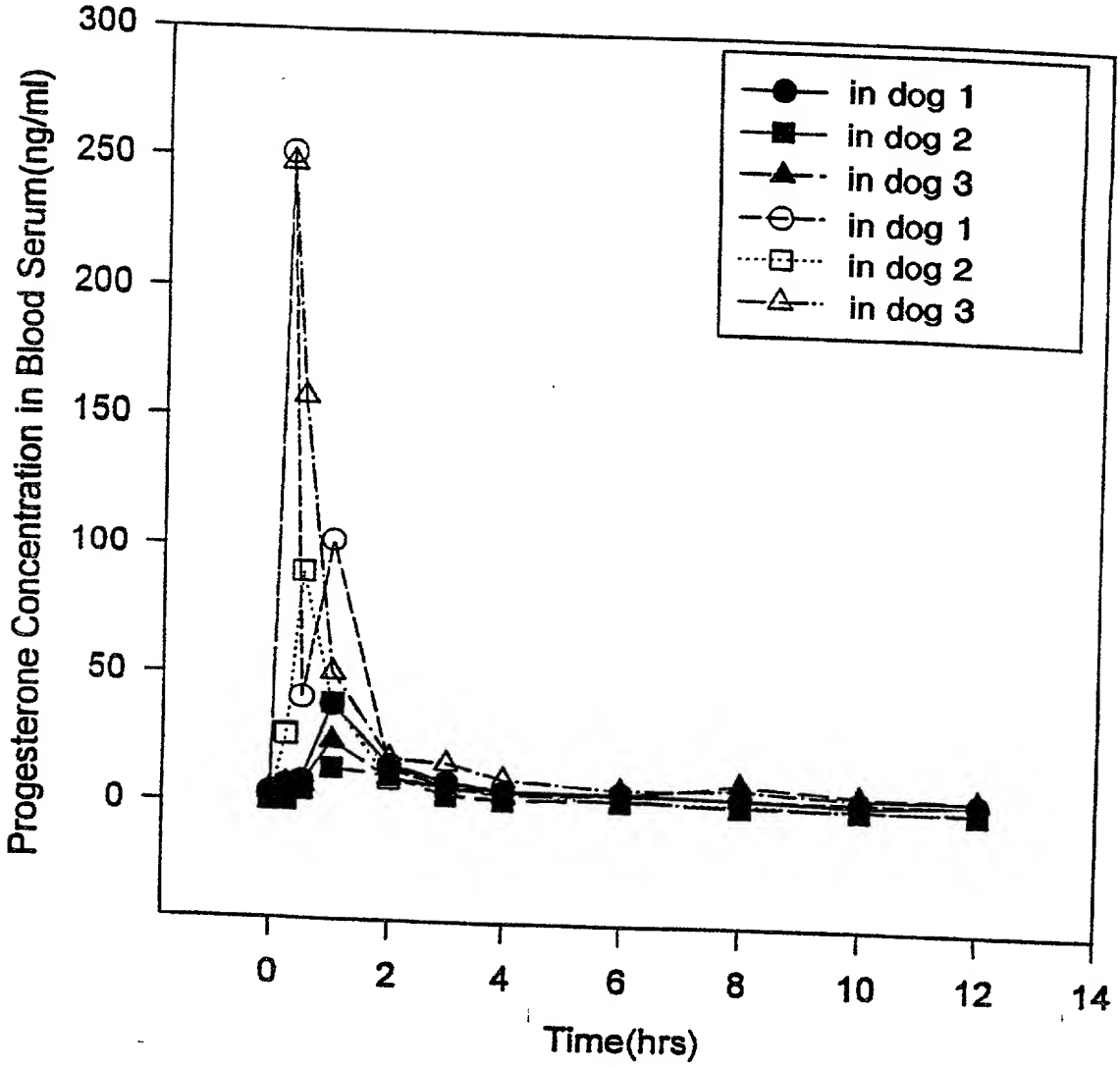
300
250
200
150
100
50
0
Progesterone Concentration in Blood Serum(ng/ml)
0
2
4
6
8
10
12
14
Time(hrs)
in dog 1
in dog 2
in dog 3
in dog 1
in dog 2
in dog 3

FIG. 12

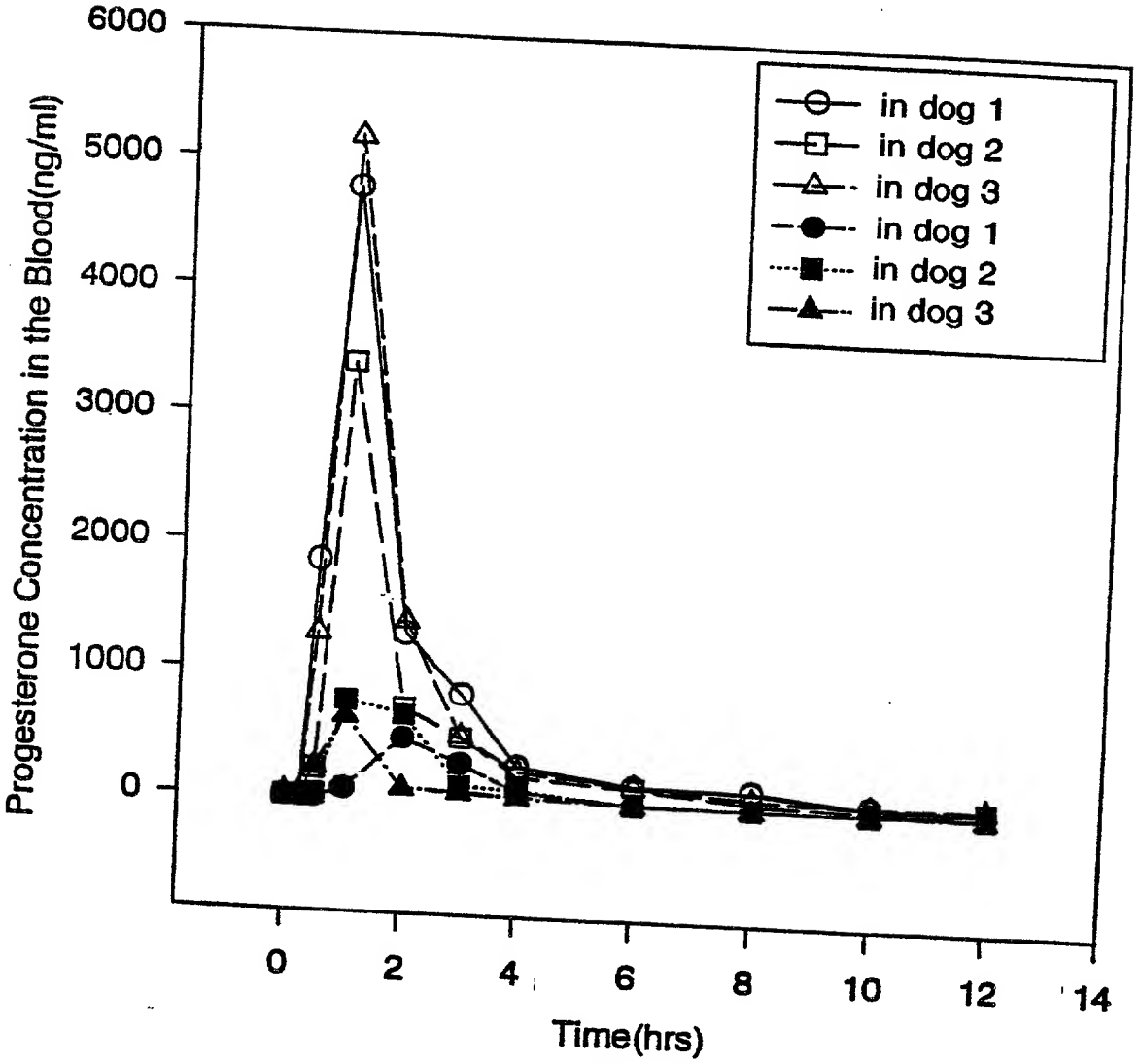
6000
5000
4000
3000
2000
1000
0
Progesterone Concentration in the Blood(ng/ml)
0
2
4
6
8
10
12
14
Time(hrs)
in dog 1
in dog 2
in dog 3
in dog 1
in dog 2
in dog 3

FIG. 13

Pharmacokinetic Data for Oral Progesterone Formulations Dosed to Dogs (40mg)

Formulation #	T_{max}(h)				C_{max}(ng/ml)				AUC (ng/ml*h)			*Relative BA % Average (s.d)
	Dog 1	2	3	Avg	Dog 1	2	3	Avg (s.d).				
1	1	1	1	1	38.4	13.9	24.4	25.6(12.3)	104	51	104	100
2	0.25	0.50	0.25	0.33	252	90.8	248	197(92)	226	113	265	232 (21)
3	0.50	0.25	0.50	0.42	53.4	57.7	33.7	48.3(12.8)	109	95	102	130 (50)
4	0.5	1	1	0.83	174	57.1	30.4	87.2(76.4)	167	289	73	176(108)
5	0.5	1	0.25	0.58	57.2	70.8	74.7	67.5(9.1)	114	342	86	181(141)

AUC is calculated by trapezoidal rule from time zero to the last blood sampling point (12h).
The relative bioavailability is the ratio of AUC for liquid formulations to that for laqueus drug–layer formulation.

Formulation Composition (wt%)

Components	Formulation #				
	1	2	3	4	5
Progesterone	60	4	4	4	4
Mannitol	21				
Ac-di-sol	10				
Myji 52-s	5				
HPMC E-5	3				
Mg stearate	1				
Cremophor EL		48	96		48
Myvacet 9-45		48		96	
Olive oil					48

FIG. 14

Pharmacokinetic Data for Emulsion Progesterone Formulation and Nonemulsion Push-Pill Drug-Layer Formulation (300mg dose)

Formulation #	T_{max}(h)				C_{max}(ng/ml)				AUC (ng/ml*h)				Relative BA (%) Average (s.d)
	Dog 1	2	3	Avg	Dog 1	2	3	Avg (s.d).	Dog 1	2	3	Avg.(s.d)	
Nonemulsion	2	1	1	1.33	489	778	649	639(145)	1101	1715	898	1238(425)	100
Emulsion	1	1	1	1	4800	3420	5180	4467(926)	7715	4708	7418	6614(1657)	600 (289)

AUC is calculated by trapezoidal rule from time zero to the last blood sampling point (12h).
The relative bioavailability is the ratio of AUC for liquid formulations to that for MPA-22 drug-layer formulation.

Formulation Composition (wt%)

Components	Nonemulsion Drug-Layer	Emulsion Oral Formulation
Progesterone	60	50
Mannitol	21	
Ac-di-sol	10	
Myji 52-s	5	12.5
HPMC E-5	3	
Mg stearate	1	
Cremophor EL		25.0
Myvacet 9-45		12.5

FIG. 15